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Applicants have amended the claims to encompass more particular compounds ie., oligomers that include furanose ($X=O$), and a biradical defined by R^{4*} and R^{2*} . The specific biradical structure now claimed consists of 2-5 atoms that are selected from more particular oxy groups as shown in amended claim 141.

Support for the claim amendments can be found throughout the instant application including the Drawings and claims as filed originally.

Particular support for the biradical language introduced into claim 141 can be found in claim 151 as filed originally (now cancelled) and on pg. 8, line 24 to pg. 11. See also pg. 25, lines 12-27.

The amendment to claim 160 specifies intended nucleobases more particularly. Support can be found on page 16, line 14-19, for instance. See also the cited U.S patent to Benner et al. on pg. 16.

The amendments to claims 154, 156, 159, 176, and 177 are intended to improve claim form and/or dependency.

No new matter has been added by virtue of the claim amendments.

Early consideration and allowance of the amended claims would be most appreciated.

Directly attached to this submission is a marked up version to show changes made.

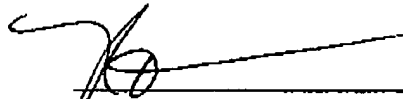
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Although it is not believed that any fee is needed the consider this submission, the USPTO is hereby authorized to charge deposit account no. 04-1105 if such a fee is deemed necessary.

Respectfully submitted,

Date:

2/25/03



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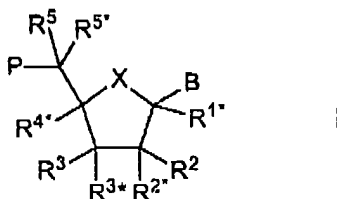
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MARKED UP VERSION TO SHOW CHANGES MADE

Claims 142, 143, 150-153, 155, 157, 158, 161-172, 193, and 203-208 were canceled without prejudice.

Claims 141, 154, 156, 159, 160, 176, 177, and 195 were amended as follows:

141. (Amended) An oligomer comprising at least one LNA nucleoside of the general formula I



wherein X is selected from -O-, [-S-, -N(R^{N*})-, -C(R⁶R^{6*})-, -O-C(R⁷R^{7*})-, -C(R⁶R^{6*})-O-, -S-C(R⁷R^{7*})-, -C(R⁶R^{6*})-S-, -N(R^{N*})-C(R⁷R^{7*})-, -C(R⁶R^{6*})-N(R^{N*})-, and -C(R⁶R^{6*})-C(R⁷R^{7*})-];

B is selected from hydrogen, hydroxy, optionally substituted C₁₋₄-alkoxy, optionally substituted C₁₋₄-alkyl, optionally substituted C₁₋₄-acyloxy, nucleobases, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands;

P designates the radical position for an internucleoside linkage to a succeeding monomer, or a 5'-terminal group, such internucleoside linkage or 5'-terminal group optionally including the substituent R⁵:

one of the substituents R^2 , R^{2*} , R^3 , and R^{3*} is a group P^* which designates an internucleoside linkage to a preceding monomer, or a 3'-terminal group;

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one pair [or two pairs] of non-geminal substituents [selected from the present substituents of R^{1*}] R^{4*} , [R^5 , R^{5*} , R^6 , R^{6*} , R^7 , R^{7*} , R^{N*} ,] and [the ones of R^2] R^{2*} , [R^3 , and R^{3*} not designating P^* each designates] designating a biradical consisting of [1-8] 2-5 groups/atoms selected from [-C(R^a)(R^b)-, -C(R^a)=C(R^b)-, -C(R^a)=N-, -O-, -Si(R^a)₂-, -S-, -SO₂-, -N(R^a)-, and >C=Z,

wherein Z is selected from -O-, -S-, and -N(R^a)-, and R^a and R^b each is independently selected from hydrogen, optionally substituted C₁₋₁₂-alkyl, optionally substituted C₂₋₁₂-alkenyl, optionally substituted C₂₋₁₂-alkynyl, hydroxy, C₁₋₁₂-alkoxy, C₂₋₁₂-alkenyloxy, carboxy, C₁₋₁₂-alkoxycarbonyl, C₁₋₁₂-alkylcarbonyl, formyl, aryl, aryloxy-carbonyl, aryloxy, arylcarbonyl, heteroaryl, heteroaryloxy-carbonyl, heteroaryloxy, heteroarylcarbonyl, amino, mono- and di(C₁₋₆-alkyl)amino, carbamoyl, mono- and di(C₁₋₆-alkyl)-amino-carbonyl, amino-C₁₋₆-alkyl-aminocarbonyl, mono- and di(C₁₋₆-alkyl)amino-C₁₋₆-alkyl-aminocarbonyl, C₁₋₆-alkyl-carbonylamino, carbamido, C₁₋₆-alkanoyloxy, sulphonyl, C₁₋₆-alkylsulphonyloxy, nitro, azido, sulphonyl, C₁₋₆-alkylthio, halogen, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands, where aryl and heteroaryl may be optionally substituted, and where two geminal substituents R^a and R^b together may designate optionally substituted methylene (=CH₂), and wherein two non-geminal or geminal substituents selected from R^a , R^b , and any of the substituents R^{1*} , R^2 , R^{2*} , R^3 , R^{3*} , R^{4*} , R^5 , R^{5*} , R^6 and R^{6*} , R^7 , and R^{7*} which are present and not involved in P, P^* or the biradical(s) together may form an associated biradical selected from biradicals of the same kind as defined before;

said pair(s) of non-geminal substituents thereby forming a mono- or bicyclic entity together with (i) the atoms to which said non-geminal substituents are bound and (ii) any intervening atoms] -(CR^{*}R^{*})_r-Y-(CR^{*}R^{*})_s-, -(CR^{*}R^{*})_r-Y-(CR^{*}R^{*})_s-Y-, -Y-(CR^{*}R^{*})_r+s-Y-, -Y-(CR^{*}R^{*})_r-Y-(CR^{*}R^{*})_s-, -(CR^{*}R^{*})_r+s-, each R^{*} is independently selected from hydrogen, halogen, hydroxy, mercapto, amino, optionally substituted C₁₋₆-alkoxy, optionally substituted

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~~C₁₋₆-alkyl, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands, Y is -O-, -S-, 0 (zero) or -N(RN)-, and each of r and s is 0-4 with the proviso that the sum r+s is 1-4, and provided that when the biradical is - (CR^{*}R^{*})_r-Y-(CR^{*}R^{*})_s-, then Y is -S- or -N(RN^{*})-; and~~
each of the substituents R^{1*}, R², [R^{2*}], R³, [R^{4*}], R⁵, R^{5*}, [R⁶] and R^{6*}, [R⁷] and R^{7*} which are present and not involved in P, P^{*} [or the biradical(s)] is independently selected from hydrogen, optionally substituted C₁₋₁₂-alkyl, optionally substituted C₂₋₁₂-alkenyl, optionally substituted C₂₋₁₂-alkynyl, hydroxy, C₁₋₁₂-alkoxy, C₂₋₁₂-alkenyloxy, carboxy, C₁₋₁₂-alkoxycarbonyl, C₁₋₁₂-alkylcarbonyl, formyl, aryl, aryloxy-carbonyl, aryloxy, arylcarbonyl, heteroaryl, heteroaryloxy-carbonyl, heteroaryloxy, heteroarylcarbonyl, amino, mono- and di(C₁₋₆-alkyl)amino, carbamoyl, mono- and di(C₁₋₆-alkyl)-amino-carbonyl, amino-C₁₋₆-alkyl-aminocarbonyl, mono- and di(C₁₋₆-alkyl)amino-C₁₋₆-alkyl-aminocarbonyl, C₁₋₆-alkyl-carbonylamino, carbamido, C₁₋₆-alkanoyloxy, sulphonyl, C₁₋₆-alkylsulphonyloxy, nitro, azido, sulphonyl, C₁₋₆-alkylthio, halogen, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands, where aryl and heteroaryl may be optionally substituted[, and where two geminal substituents together may designate oxo, thioxo, imino, or optionally substituted methylene, or together may form a spiro biradical consisting of a 1-5 carbon atom(s) alkylene chain which is optionally interrupted and/or terminated by one or more heteroatoms/groups selected from -O-, -S-, and -(NR^N)- where R^N is selected from hydrogen and C₁₋₄-alkyl, and where two adjacent (non-geminal) substituents may designate an additional bond resulting in a double bond; and R^{N*}, when present and not involved in a biradical, is selected from hydrogen and C₁₋₄-alkyl];

and basic salts and acid addition salts thereof.;

with the proviso that,

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- (ii) R^3 and R^5 do not together designate a biradical selected from $-\text{CH}_2-\text{CH}_2-$, $-\text{O}-\text{CH}_2-$, when LNA is a bicyclic nucleoside analogue;
- (iii) R^3 , R^5 , and R^{5*} do not together designate a triradical $-\text{CH}_2-\text{CH}(-)-\text{CH}_2-$ when LNA is a tricyclic nucleoside analogue;
- (iv) R^{1*} and R^{6*} do not together designate a biradical $-\text{CH}_2-$ when LNA is a bicyclic nucleoside analogue; and
- (v) R^{4*} and R^{6*} do not together designate a biradical $-\text{CH}_2-$ when LNA is a bicyclic nucleoside analogue.]

154. (Amended) An oligomer of claim [153] 151 wherein R^{3*} designates P^* .

156. (Amended) An oligomer of claim [155] 154 wherein [X is O], R^2 is selected from hydrogen, hydroxy, and optionally substituted C_{1-6} -alkoxy, and R^{1*} , R^3 , R^5 , and R^{5*} designate hydrogen.

159. (Amended) An oligomer of claim [155] 156 wherein B is selected from nucleobases.

160. (Amended) An oligomer of claim 159 wherein the oligomer comprises at least one LNA nucleoside wherein B is selected from adenine, guanine, thymine, cytosine, [and] uracil, ~~purine, xanthine, diaminopurine, 8-oxo- N^6 -methyladenine, 7-deazaxanthine, 7-deazaguanine, N^4 , N^4 -ethanocytosine, N^6 , N^6 -ethano-2,6-diaminopurine, 5-methylcytosine, 5-(C^3 - C^6)-alkynylcytosine, 2,6-diaminopyrimidine, 2,6-diaminopyrazine, 1-methyl-pyrazolo[4,3-d]pyrimidine-5,7(4H,6H)-dione, 1-methyl-pyrazolo[4,3-d]pyrimidine-5,7(4H,6H)-dione, 5-fluorouracil, 5-bromouracil, pseudoisocytosine, 2-hydroxy-5-methyl-4-triazolopyridine, isocytosine, isoguanine, and inosine.~~

176. (Amended) An oligomer of claim 141 wherein each of the substituents R^{1*} , R^2 , [R^{2*}], R^3 , R^{3*} , [R^{4*}], R^5 , R^{5*} , R^6 , R^{6*} , R^7 , and R^{7*} of the one or more LNA nucleosides, which are

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present and not involved in P, P^* [or the biradical(s)], is independently selected from hydrogen, optionally substituted C_{1-6} -alkyl, optionally substituted C_{2-6} -alkenyl, hydroxy, C_{1-6} -alkoxy, C_{2-6} -alkenyloxy, carboxy, C_{1-6} -alkoxycarbonyl, C_{1-6} -alkylcarbonyl, formyl, amino, mono- and di(C_{1-6} -alkyl)amino, carbamoyl, mono- and di(C_{1-6} -alkyl)-amino-carbonyl, C_{1-6} -alkyl-carbonylamino, carbamido, azido, C_{1-6} -alkanoyloxy, sulphonyl, sulphonyl, C_{1-6} -alkylthio, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands, and halogen, where two geminal substituents together may designate oxo, and where R^{N*} , when present and not involved in a biradical, is selected from hydrogen and C_{1-4} -alkyl.

177. (Amended) An oligomer of claim 141 wherein [X is selected from -O-, -S-, and -NR^{N*}-, and] each of the substituents $R^{1*}, R^2, [R^{2*},] R^3, R^{3*}, [R^{4*},] R^5, R^{5*}, R^6, R^{6*}, R^7$, and R^{7*} of the LNA(s), which are present and not involved in P, P^* [or the biradical(s),] designate hydrogen.

195. (Amended) A diagnostic or analysis kit comprising an oligonucleotide of claim [193] 141.

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